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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,193	05/04/2006	Karin Cabrera	MERCK-3160	8428
23599 7590 01/06/2009 MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201				
EXAMINER KENNEDY, TIMOTHY J				
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1791				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/578,193

**Applicant(s)**

CABRERA ET AL.

**Examiner**

TIMOTHY KENNEDY

**Art Unit**

1791

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 17 December 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Response to Amendment***

***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
3. Claims 1-5, 7, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizuka et al (Preparation and Chromatographic Application of Macroporous Silicate in a Capillary), in view of Eguchi et al (U.S. Patent 5,145,579) and Tanaka et al (Monolithic silica columns for high-efficiency chromatographic separations).
4. Regarding Claim 1, Ishizuka et al teach:

5. Process for the production of monolithic porous moldings which completely fill their gelling mould (Bottom of 2nd column page 371 - Top of 1st column page 372; and Top of 1st column page 374)
6. Provision of a gelling mould (Figure 1 page 372)
7. Activation of the gelling mould by surface etching (Middle of 2nd paragraph 1st column page 372: 1 M NaOH solution. This would naturally increase the surface area of the mold wall)
8. Filling of the gelling mould with monomer sol (2nd paragraph 1st column page 372: A silica rod ... overnight at 40° C)
9. Polymerization of the monomer sol and aging of the resultant gel for the formation of pores (2nd paragraph 1st column page 372: A silica rod ... overnight at 40° C)
10. However, Ishizuka et al do not teach the activation of the gelling mould by chemical modification. This is done to better adhere the sol-gel to the inner mould wall.
11. In the same field of endeavor, Eguchi et al teach the use of 3-(methacyloxy)propyltrimethoxysilane as a treatment for a capillary wall.
12. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the 3-(methacyloxy)propyltrimethoxysilane as taught by Eguchi et al, in the Ishizuka method to activate the inner wall of the mould for better sol-gel adhesion.
13. Ishizuka et al and Eguchi et al do not teach:
14. The monolithic porous molding produced has an internal diameter of 0.5-50 mm

15. In the same field of endeavor, Tanaka et al teach monolithic porous silica columns with diameters of 7, 4.6, and 0.1 mm (Table 2, page 41).

16. It would have been obvious to one having ordinary skill in the art at the time of the invention was made to use the diameters as taught by Tanaka et al, using the previous method of Ishizuka et al and Eguchi et al, since a larger diameter column is known to have a larger loading capacity, enabling the user to filter a larger amount of material.

17. Regarding claim 2, Ishizuka et al further teach:

18. A gelling mould made from glass, glass-coated stainless steel or fused silica (Figure 1 page 372)

19. Regarding claim 3, Ishizuka et al and Tanaka et al do not teach the use of alkoxysilanes, organoalkoxysilanes, or slurries of particles to increase the surface area of the inner mould wall.

20. In the same field of endeavor, Eguchi et al teach the use of 3-(methacyloxy)propyltrimethoxysilane (column 6 lines 48-60), which is a member of the organoalkoxysilane family. This would increase the surface area of the mold wall, thus allowing a stronger molecular bond between the mold and the molding.

21. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the 3-(methacyloxy)propyltrimethoxysilane as taught by Eguchi et al, using the Ishizuka et al and Tanaka et al method to increase the surface area of the inner mould wall, thus allowing a stronger molecular bond between the mold and the molding.

22. Regarding claim 4, Ishizuka et al and Tanaka et al do not teach the use of a bifunctional reagent to chemically modify the inner mould wall.
23. In the same field of endeavor, Eguchi et al teach the use of bifunctional reagents (column 3 lines 16-29). This would chemically modify the mold wall, thus allowing a stronger molecular bond between the mold and the molding
24. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the bifunctional reagents as taught by Eguchi et al, using the Ishizuka et al and Tanaka et al method to chemically modify the inner mould wall so that the sol-gel will mixture will have a better chemical bond with the wall ensuring minimal shrinkage.
25. Regarding claim 5, Ishizuka et al further teach:
26. A sol-gel process is used for the production of the monolithic porous moldings (2nd paragraph 1st column page 372: A silica rod ... overnight at 40° C)
27. Regarding claim 7, Ishizuka et al further teach:
28. Monolithic porous moldings which have been polymerized in their gelling mould. Using the previous combination from claim 1, it would be possible to create monolithic porous moldings which have been polymerized in their gelling mould.
29. Regarding claim 8, using the combination from claim 1:
30. Chromatographic separation of at least two substances, comprising subjecting a mixture of said at least two substances to a molding according to claim 7 (The molding produced by the previous methods would be able to separate at least two substances, which is a natural property of any chromatography tube)

31. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ishizuka et al, Eguchi et al, and Tanaka et al as applied to claim 1 above, and further in view of Zhang et al (Single step on-column frit making for capillary high-performance liquid chromatography using sol-gel technology)

32. Regarding claim 6, the previous combination teaches the method of claim 1, but does not teach the use of particles, fibers, or organoalkoxysilane in the sol-gel to reduce shrinkage.

33. In the same field of endeavor, Zhang et al teach the use of methyltriethoxysilane (a known organoalkoxysilane) in sol-gel for use in chromatography columns ( top of column 2, page 15. As taught by Zhang et al the addition of methyltriethoxysilane to the sol gel would result in improved mechanical properties, such as flexibility, ductility, and elasticity. The addition of methyltriethoxysilane to the sol gel also would result in a stronger bond with the column wall. The addition of an organoalkoxysilane such as methyltriethoxysilane to the sol gel will result in less shrinkage, since it has been shown that the addition of such a chemical results in a more flexible material that is less likely to come off of the column wall.

34. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the organoalkoxysilane as taught by Zhang et al, using the previous method as taught by Ishizuka et al, Eguchi et al, and Tanaka et al since it has been shown that the addition of such a chemical results in a more flexible material that is less likely to separate from the column wall.

***Response to Arguments***

35. Applicant's arguments filed 12/02/2008 with respect to claims 1-8 have been considered but are moot in view of the new ground(s) of rejection as shown above. Applicant argues that Ishizuka et al and Eguchi et al do not teach a column having a diameter between 0.5 and 50 mm, or how the shrinkage of the molding is controlled. As necessitated by the amendments to the claims, Tanaka et al shows the production of chromatography columns between 0.1 and 7 mm in diameter. The combination of Ishizuka et al, Eguchi et al, Tanaka et al, and Zhang et al illustrates that molding shrinkage would be controlled due to, and as such it would have been obvious to one having ordinary skill in the art that:

- a. Etching the mold (thus increasing the surface area) using NaOH, increasing the surface area using 3-(methacyloxy)propyltrimethoxysilane, or chemically modifying the wall using bifunctional reagents. This allows for better adhesion with the molding to the mold wall, which would help reduce shrinkage in the final product.
- b. As well with the addition of an organoalkoxysilane, such as methyltriethoxysilane to the sol-gel, which would aid in reducing shrinkage of the molding since it is known that the addition of methyltriethoxysilane to a sol-gel for use in chromatography columns will increase mechanical properties (ductility, flexibility, and elasticity) and produce a stronger bond with the mold wall. Thus reducing the likelihood of shrinkage or separation from the mold wall.



36. The Applicant's arguments are not persuasive, since the applicant has failed to show specifically why it would not have been obvious for one of ordinary skill in the art to produce a chromatography molding that does not separate from its mold wall even when the method and materials from pertinent sources teach that it is possible to create such a molding.

### ***Conclusion***

37. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

38. U.S. Patent 4,017,528 (Already of Record): organoalkoxysilanes

39. U.S. Patent 4,169,790: Increasing the surface area of the inner wall of a chromatography column

40. U.S. Patent 4,376,641: Etching the inner wall and coating the inner wall of a chromatography column

41. U.S. Patent 4,865,707: The use of bifunctional reagents to activate the inner wall of a chromatography column

42. U.S. Patent 5,637,135: Coating the inner wall with alkoxysilane

43. Frantisek Svec, Eric C. Peters, David Sykora, Jean M.J. Frechet; Design of the monolithic polymers used in capillary electrochromatography columns, July 2000, Journal of Chromatography A, volume 887, pages 3-29:

44. Etching the inner wall for better sol-gel adherence

45. Japan Published Patent Application JP 2002293657: The use of particles in the sol-gel (Already of Record)

46. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

47.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY KENNEDY whose telephone number is (571) 270-7068. The examiner can normally be reached on Monday to Friday 9:00am to 6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Del Sole can be reached on (571) 272-1130. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tjk

/Joseph S. Del Sole/

Supervisory Patent Examiner, Art Unit 1791